

Unlocking erlotinib's full potential

A new frontier in lung cancer therapy

- Lung cancer presents significant treatment challenges due to limited effectiveness and adverse effects of current therapies.
- Targeted therapies like erlotinib offer promise but come with adverse effects like interstitial lung disease, complicating treatment.
- Can treatment strategies be optimised to minimise adverse effects and improve patient outcomes with targeted therapies like erlotinib?
- A new protocol developed by Dr Songphol Tungjitviboonkun (Department of Medicine, Sirindhorn Hospital, Bangkok) has the potential to significantly impact the management and safety of erlotinib, offering a safe and more effective lung cancer treatment.

Lung cancer remains a challenge worldwide, claiming many lives each year. Non-small-cell lung cancer (NSCLC) is the most common type of lung cancer, and accounts for approximately 85% of all lung cancer cases. Treatment outcomes are poor in patients who present with advanced or spreading ('metastatic') NSCLC cancer, with chemotherapy offering only symptomatic relief and modest improvements in survival. Dr Tungjitviboonkun at the Department of Medicine, Sirindhorn Hospital in Bangkok, sheds light on critical aspects of lung cancer treatment, particularly concerning adverse events associated with erlotinib – a medication used in the treatment NSCLC. His research aims to better understand and manage these adverse effects. In this way, he offers valuable insights into optimising the

use of targeted therapies while minimising potential risks.

Lung cancer and our weapons against it

Lung cancer is a significant global health concern, accounting for a substantial portion of cancer-related deaths worldwide. Its incidence and mortality rates are closely tied to factors such as tobacco use, industrialisation, and environmental exposures. Despite advancements in existing treatments, the prognosis for patients with lung cancer remains poor, particularly in cases of advanced or metastatic disease. NSCLC constitutes the majority of lung cancer cases, and targeted therapies like erlotinib have emerged as promising options. However, challenges persist in the management of lung cancer,

Under the right conditions, and with careful monitoring, it might be safe to try using erlotinib again in certain patients.

including the development of resistance to targeted therapies and the need for personalised treatment approaches tailored to individual patients' molecular profiles.

Erlotinib, marketed under the brand name Tarceva, represents a significant advancement in the treatment of NSCLC. Erlotinib specifically targets the tyrosine kinase activity of epidermal growth factor receptor (EGFR). Tyrosine kinases are enzymes that transfer phosphate groups to tyrosine residues on target proteins, thereby activating or deactivating them. By blocking the tyrosine kinase activity of EGFR, erlotinib halts the downstream signalling pathways that promote cancer cell growth and survival. This targeted approach stops the abnormal signalling pathways involved in cancer progression, ultimately slowing tumour growth, and possibly causing tumours to shrink or stabilise.

The Achilles' heel of erlotinib

The approval of erlotinib as a first-line therapy for patients with locally advanced or metastatic NSCLC carrying EGFR-activating mutations marks a significant shift in treatment approaches, allowing for personalised care. Clinical trials have showcased its effectiveness in extending progression-free survival and enhancing response rates compared to traditional platinum-based chemotherapy, particularly among Caucasian and Asian populations. However, despite its benefits, erlotinib is associated with notable side effects, including rash and diarrhoea. Importantly, erlotinib is also linked with serious cases of interstitial lung disease. Interstitial lung disease involves inflammation and scarring of lung tissue, making the lung tissue stiff which impairs breathing.

Interstitial lung disease has been linked to patient fatalities, raising serious concerns about the safety of the drug itself. Drawing from his clinical experience, Dr Tungjitviboonkun believes that not all cases of interstitial pneumonitis are caused by erlotinib. Instead, some patients may experience temporary conditions during their lung disease that

make their lungs more sensitive. If this is the case, then – under the right conditions and with careful monitoring – Dr Tungjitviboonkun suggests that it could be safe to try using the drug again in these patients. Indeed, many patients can't afford the expensive alternative second-line medications to erlotinib.

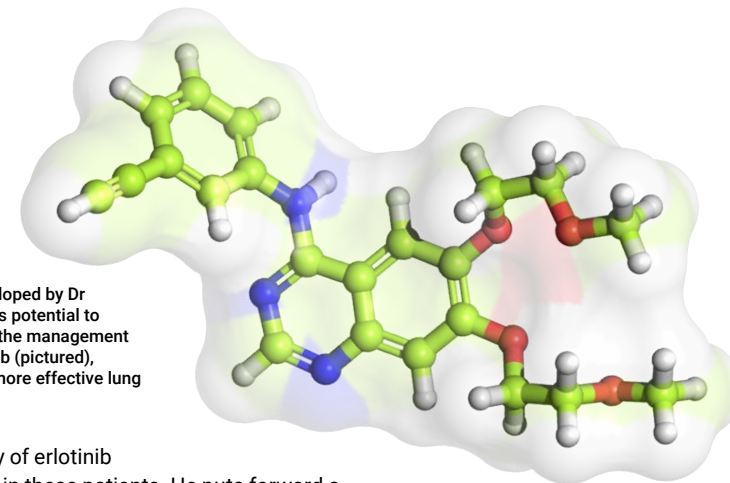
Dr Tungjitviboonkun set out to investigate whether different medication strategies and management techniques could help patients recover from interstitial pneumonitis safely and effectively. In particular, he wanted to test whether it's possible for some patients to take erlotinib again, but with close medical supervision. He explains, 'This approach of rechallenging the medication can be a good option and may even help prolong the patient's life compared to switching back to conventional chemotherapy alone.'

The potential of erlotinib

In a recent study published in the *Journal of Oncology Pharmacy Practice*, Dr Tungjitviboonkun describes the development of an innovative treatment protocol for patients with interstitial lung pneumonitis caused by erlotinib. The study involved a 64-year-old patient diagnosed with advanced-stage adenocarcinoma of the lung with brain metastasis. Dr Tungjitviboonkun investigated the adverse effects of erlotinib and explored its potential benefits for the patient, with close clinical observation. The patient had previously received erlotinib as a first-line therapy. However, after two weeks of treatment, he developed symptoms of interstitial lung disease, which was suspected to be associated with erlotinib use. Adverse effects included diarrhoea, rash, acute renal failure, cardiac arrhythmia, hepatotoxicity, and pulmonary toxicity. The patient was quickly diagnosed after the onset of interstitial pneumonitis, erlotinib was withdrawn immediately and the patient was treated with corticosteroids. The patient recovered successfully and after two months, erlotinib was readministered. The patient was closely monitored and showed stable disease progression, remaining stable after two months of careful follow up.

An innovative protocol

This study is the first report of erlotinib rechallenge with no development of interstitial pneumonitis following readministration of the drug. Dr Tungjitviboonkun suggests that some cases of lung disease may be transient and unrelated to the drug itself, allowing



A new protocol developed by Dr Tungjitviboonkun has potential to significantly impact the management and safety of erlotinib (pictured), offering a safe and more effective lung cancer treatment.

for the possibility of erlotinib readministration in these patients. He puts forward a strong case for this new treatment protocol for interstitial lung pneumonitis caused by erlotinib, highlighting that a swift diagnosis, cessation of erlotinib, and timely treatment with corticosteroids are important for a positive outcome. This innovative approach has the potential to significantly impact the management and safety of erlotinib treatment for NSCLC patients.

Targeted and personalised treatment

Lung cancer continues to pose significant health burdens worldwide, and Dr Tungjitviboonkun's study represents an innovative and crucial step forward in the quest for safer and more effective treatments for the disease. He believes that the reasons why some patients develop interstitial pneumonitis while taking erlotinib are varied. If this is true, it could lead to a change in practice of erlotinib readministration. Under the right conditions and with careful monitoring, the drug can be safely given again in certain patients. By addressing these challenges, Dr Tungjitviboonkun's work paves the way for safer and more effective treatments for lung cancer patients.

Personal response

How do you think your research findings will impact the current standard of care for lung cancer patients receiving targeted therapies like erlotinib?

Erlotinib-associated pneumonitis, though rare, carries with it a staggering mortality rate of over 80 percent. However, my research offers a glimmer of hope by reporting successful treatment outcomes where patients not only survived but also avoided further morbidity. I firmly believe that my work has the potential to lay the foundation for future treatment schemes, particularly in light of the increasing prevalence of lung cancer and the growing demand for erlotinib therapy.

Moreover, in resource-limited or developing countries, access to second-line therapy is often severely restricted. When patients experience side effects from targeted therapy, they are frequently left with no choice but to revert to conventional chemotherapy instead of higher-tier targeted therapies. Unsurprisingly, the overall survival of these patients is significantly shorter compared to those who have access to more advanced treatments.

Just imagine the impact if we could offer these patients the opportunity to rechallenge the medication and extend their survival, allowing them to cherish more precious moments with their families instead of enduring the debilitating side effects of chemotherapy during their final days. Though it may seem like a modest step, it holds the promise of making a profound difference in the landscape of lung cancer care.

What are the next steps for your research?

The next steps for my research involve focusing on identifying parameters, such as genetic polymorphism, ethnicity, and age, that can indicate which patients can successfully undergo rechallenge with targeted therapy. This is crucial for developing personalised treatment schemes tailored to individual patients' needs. By pinpointing specific indicators or biomarkers, we aim to refine patient selection criteria and optimise the efficacy and safety of rechallenging targeted therapies like erlotinib. This personalised approach holds the potential to revolutionise how we manage lung cancer patients, ensuring that treatment decisions are based on factors unique to each individual, ultimately leading to better outcomes and improved quality of life.

Details



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Bio

Songphol Tungjitviboonkun, MD, is a haematologist and researcher based in Bangkok, Thailand. Trained at Chulalongkorn University, his research primarily focuses on haematology. He is a member of several professional societies, including the European Society for Medical Oncology and the American Medical Association. Since 2023, he has been elected to serve on the National Hemovigilance Committee of the Thai Red Cross Society.

Further reading

Tungjitviboonkun, S, Bumrungratanayos, N, Jitwimungsanon, J, (2024) [Erlotinib-associated interstitial pneumonitis with successful readministration](#). *Journal of Oncology Pharmacy Practice*, 30(1), 206–209.

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